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EXAMINER	
LANDAU, SHARMILA GOLLAMUDI	
ART UNIT	PAPER NUMBER
1616	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/24/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s).	
	09/913,752	FERCEJ TEMELJOTOV ET AL.	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *61-81* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *61-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Amendments/Remarks filed 2/1/07 is acknowledged. Claims **61-81** are pending in this application.

Response to Arguments

Applicant argues that Briskin fails to appreciate the significance of forming a matrix with these components to facilitate the controlled release of clarithromycin. Applicant argues that Briskin fails to teach a matrix comprising all the components.

Applicant's arguments filed 2/7/07 have been fully considered but they are not persuasive. Independent claim 61 is directed to a pharmaceutical composition comprising a fatty component; a hydrophilic component, dispersed within the matrix, and clarithromycin dispersed within a matrix. Briskin discloses an oral composition containing 43.4% clarithromycin, 5.5% povidone, 26% carbopol, 5% hydroxypropylcellulose (an alkyl-substituted cellulose ether), 10% glyceryl behenate, and 10% microcrystalline cellulose. See table 1 on page 8. The examiner notes applicant's argues that Briskin does not teach a matrix; however the examiner disagrees. The examiner points out that instant application discloses on page 7, that the instant invention is made by mixing all the ingredients together, sieving, and compressing to form a tablet. The examiner points out that Briskin discloses on page 6, the method of making the tablet wherein the *all* the ingredients are blended thoroughly, granulated, and then the particles are formed into tablets. Thus, Briskin discloses all the claimed components, which are mixed together to form a matrix. Therefore, the instant claims are not structurally distinguishable from the prior art.

Applicant argues that Briskin fails to provide a motivation to use hydrophilic polymers in conjunction with fatty components.

The examiner points out that Briskin clearly discloses the use of hydroxypropylcellulose and thus anticipates the claimed invention. Therefore, a motivation is not required since the rejection is made under anticipation.

Applicant argues that Gibson and Evenstad do not remedy the deficiencies of Briskin. Applicant argues there is no motivation to experiment with hydrophilic polymers as fatty components to provide a matrix. Applicant argues the examiner has relied upon impermissible hindsight.

The examiner has discussed the merits of Briskin above. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Firstly, the examiner points out that the Briskin discloses the use of a hydrophilic polymer, in particular hydroxypropylcellulose (HPC), in combination with a fatty component. Additionally, Briskin discloses the use of various hydrophilic binders including HPC to retard release. Therefore, Gibson is only relied upon to teach the functional equivalency of HPC and HPMC as hydrophilic polymers since the Briskin document itself suggests the combination of a hydrophilic polymer and a fatty component. Applicant has not addressed this argument. With regard to Evenstad, Briskin teaches the use of a hydrophilic binder and Evenstad teaches that low viscosity HPMC are used if the purpose is to utilize HPMC as a binder. Therefore, the examiner has made

a reasonable motivation to specifically utilize a low viscosity cellulose polymer and applicant has not addressed this.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 79 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 79 depends on claim 78, which is directed to an acid resistant coating. Claim 79 is directed the acid resistant coating comprising a mixture of HPMC and HPC. Applicant does not have sufficient support for this limitation. The originally filed specification, pages 6-7, provides support for the acid resistant coating comprising HPMC-phthalate and a lacquered coating comprising a mixture of HPMC and HPC. However, the specification does not provide support for an *acid resistant coating* comprising a mixture of HPC and HMPC specifically.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 79 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 79 is directed the acid resistant coating comprising a mixture of HPMC and HPC. Although hydroxypropylmethylcellulose *phthalate* is an acid resistant polymer, HPMC and HPC are not acid resistant polymers. Further clarification is requested.

Although HPMC and HPC are not rejected as indefinite, the examiner suggests applicant define the term and then use the abbreviation. For instance, hydroxypropylmethylcellulose (HPMC).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 61-63, 65-66, 68, 72, 76-77 are under 35 U.S.C. 102(b) as being anticipated by US patent 5,707,646 to Yajima et al.

Yajima et al disclose taste masking pharmaceutical compositions in the form of tablets, capsules, dry powders, and syrup. See column 3, lines 47-50. Yajima et al teach a taste-masking polymer in a low-melting substance, which is in a concentration of 10-70%. The polymer is Eudragit E and the low-melting substance includes paraffin, wax, hydrogenated oil, palmitic acid, stearic acid, stearyl alcohol, sorbitan fatty esters, and glycerin fatty esters, etc. see column 2, line 45 to column 3, line 5. Yajima et al disclose the use of excipients, binders including hydroxypropylmethyl cellulose (HPMC), polyvinyl pyrrolidone, gelatin, ethyl cellulose, etc., lubricants, surfactants, and coating agents.

Specifically example 2 discloses 600g (19.98%) of stearyl acid (fatty component), 100g Eudragit, 300g (10%) clarithromycin, 100g sorbitol, 100g xylitol, 347g mannitol, 50g maltitol, and 70g (7%) magnesium oxide (adsorbant). Example 4 discloses a composition comprising glyceryl monostearate (fatty component), Eudragit E, clarithromycin, mannitol, carboxymethylcellulose (hydrophilic component), magnesium oxide, starch, and hydroxypropylcellulose (hydrophilic component). Example 5 utilizes a hydrogenated oil. All the components are mixed together to form the oral composition. See column 3, lines 45-51.

Regarding claim, 65, since the prior art discloses the same components (a fatty component, a hydrophilic component specifically a alkyl-substituted cellulose ether, and clarithromycin), it is the examiner's position that the functional limitation of claim 65 are inherent. The examiner has provided a reasonable rationale for inherency and thus the burden has shifted to applicant to provide evidence to the contrary. Note MPEP 2112.

It should be noted that Eudragit is known as a rate controlling polymer and applicant has not provided any specific controlled release parameters; thus, Yajima is capable of providing "controlled release".

Claims 61-68, 76-78, 80-81 are under 35 U.S.C. 102(b) as being anticipated by WO 95/22319 to Briskin et al.

Briskin discloses preparing pharmaceutical composition comprising up to 90% of an active agent, 1-75% of an extrusion aid including glyceryl behenate, hydrogenated vegetable oil, fats, fatty acid esters, fatty acids, etc. The composition further contains binding agents including povidone, carboxymethylcellulose, and hydroxymethylcellulose (HMC) to retard release. See page 4-5. Briskin discloses an oral composition containing 43.4% clarithromycin, 5.5%

povidone, 26% carbopol, 5% hydroxypropyl cellulose (an alkyl-substituted cellulose ether), 10% glyceryl behenate, and 10% microcrystalline cellulose. See table 1 on page 8. The composition is then formulated in to a tablet or capsule. See page 7, line 7. On page 6, the method of making the tablet is disclosed wherein the *all* the ingredients are blended thoroughly, granulated, and then the particles are formed into tablets. Briskin discloses on page 5, lines 34-35 an enteric coating. Note that enteric coating is inherently acid resistant coating.

Regarding claim, 65, since the prior art discloses the same components (a fatty component, a hydrophilic component, and clarithromycin), it is the examiner's position that the functional limitation of claim 65 are inherent. The examiner has provided a reasonable rationale for inherency and thus the burden has shifted to applicant to provide evidence to the contrary. Note MPEP 2112.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 69, 72-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 95/22319 to Briskin et al in view of Gibson et al (5,811,120).

The disclosure of Briskin has been set forth above.

Briskin teaches the use of hydrophilic binders, specifically HMC as the hydrophilic binder, however Briskin does not the use of hydroxypropylmethylcellulose (HPMC). Further, Briskin does not teach instant surfactant.

Gibson et al teach pharmaceutical formulations containing raloxifene. Gibson et al teaches the conventional additives in pharmaceutical formulations such as hydrophilic binders. Gibson teaches the term "hydrophilic binder" represents binders *commonly used in the formulation of pharmaceuticals*, such as polyvinylpyrrolidone, polyethylene glycol, sucrose, dextrose, corn syrup, polysaccharides (including acacia, tragacanth, guar, and alginates), gelatin, and cellulose derivatives (including hydroxypropyl methylcellulose, hydroxypropyl cellulose, and sodium carboxymethylcellulose). See column 3, lines 50-60. Further, Gibson teaches the use of surfactants including sodium docosate. See column 3, lines 60-67. Further, the reference teaches that the preparation of the oral formulations is well known in the art such as direct compression. The process includes mixing the active with the hydrophilic binder and surfactant, which is then, milled if necessary, drying the granules, and compressing into tablets (col. 5, lines 10-15).

It would have been obvious of one of ordinary skill in the art at the time the invention was made to combine the teachings of Briskin et al and Gibson et al and utilize the instant hydrophilic binder (HPMC). One would have been motivated to substitute Briskin's hydrophilic

binder (cellulose derivative HMC) for instant cellulose derivative (HPMC) with a reasonable expectation of similar results since Gibson teaches that both are conventional hydrophilic binders utilized in pharmaceutical compositions. Therefore, it is prima facie obvious for a skilled artisan to substitute one functional equivalent with another known functional equivalent with the expectation of similar results and success since the art establishes that both are hydrophilic and act as binders in the composition.

Additionally, Gibson teaches the conventional use of surfactants such as instant sodium docusate in pharmaceutical compositions. Thus, the use of conventional additives in the preparation of pharmaceuticals is prima facie obvious.

Claims 70-71 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 95/22319 to Briskin et al in view of Gibson et al (5,811,120) in further view of Evenstad et al (5,126,145).

The disclosure of Briskin and Gibson have been set forth above. Briskin teaches the use of HPC as the hydrophilic *binder* and Gibson teaches the use of HPC or HPMC as the hydrophilic *binder*.

The references do not specify the viscosity of HPMC.

Evenstad teaches a controlled release tablet. Evenstad teaches the use of high viscosity HPMC to provide sustain release whereas a water-soluble pharmaceutical binder such as HPMC having binding properties has a much lower viscosity; typically a viscosity of less than 100 cps such as METHOCEL E15. See column 3, lines 5-67. METHOCEL E15 has a viscosity of 12-18 cps.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Briskin, Gibson, and Evenstad and specifically utilize a low viscosity HPMC. One would have been motivated to do so since Evenstad teaches high viscosity HPMC is useful for its sustaining action and low viscosity HPMC is useful for its binding properties. Therefore, a skilled artisan would have been motivated to utilize a low viscosity HPMC with a reasonable expectation of similar results since both Briskin and Gibson teach the use of the cellulose derivative for its binding property and Evenstad teaches the low viscosity cellulose derivative provide this function.

Claims 74-75 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 95/22319 to Briskin et al in view Curatolo et al (5,605,889).

The teaching of Briskin has been set forth above.

Although, Briskin teaches the use of conventional excipients in the composition, Briskin does not teach the use of the instant phosphate buffer.

Curatolo teaches azithromycin compositions. Curatolo teaches in addition to the active ingredient azithromycin, the tablets may be formulated with a variety of *conventional excipients* such as binders, flavorings, buffers, diluents, colors, lubricants, sweetening agents, thickening agents, and glidants. See column 6, lines 55-66. Curatolo teaches a powder composition used to make suspensions may also contain conventional optional ingredients such as a buffer to maintain a high pH upon reconstitution. Suitable buffers and pH-altering agents include anhydrous tribasic sodium phosphate, anhydrous sodium carbonate, glycine, and the like. See column 8, line 60 to column 9, line 2.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Briskin and Curatolo and utilize conventional excipients such as buffers. One would have been motivated to do so since the use of conventional additives such as buffers are routinely utilized in the art for maintaining the pH of a composition as taught by Curatolo. Thus, a skilled artisan would have been motivated to utilize a buffer to maintain the desired pH of the composition.

Claim 79 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 95/22319 to Briskin et al in view of Khan et al (5,656,296).

The disclosure of Briskin has been set forth above. Briskin teaches the composition may be coated with an enteric coating or other coatings. See page 5, lines 30-35.

Briskin does not teach a coating comprising the instant polymers.

Khan teaches a dual control sustained release drug delivery system. Khan teaches the delivery system is coated with a coating layer comprising a water insoluble polymer and water-soluble film forming polymers including cellulose derivatives such as hydroxypropylcellulose, hydroxypropyl-methylcellulose, hydroxypropylmethylcellulose phthalate, sodium carboxymethylcellulose, and the like, and mixtures thereof. See column 6, lines 30-60.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Briskin and Khan and utilize a coating layer comprising a mixture of polymers such as HPMC and HPC. One would have been motivated to do so to provide a sustained release effect. Further, a skilled artisan would have reasonably expected success since Briskin teaches the use of various coating layer.

Conclusion

All the claims are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sharmila S. Gollamudi
Primary Examiner
Art Unit 1616

SSG